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anticipated by Seigel *et al.* (Abstract, *J. Mass Spectrom.* 33:264-273 (1998)). Claims 30, 33, 36, 42, 46, 49, 54, 58, 63, 64, 67-69 and 70-75 were rejected as allegedly being obvious over Seigel *et al.* in view of Kauvar (WO89/09088).

#### Support for the Amendment

Previously pending claims 30 and 33-75 were canceled and replaced with new claims 76-90. In the new claims, the language used to refer to various components in the screening method is simplified to further clarify the claimed invention.

Support for the new claims can be found throughout the specification, claims, and drawings, as originally filed. For example, support for new claims 76, 79 and 80 can be found, *e.g.*, in originally filed claim 30 and on page 66, lines 19-20 of the specification. Support for new claim 77 can be found on, *e.g.*, page 36, lines 15-17 of the specification. Support for new claim 78 can be found on, *e.g.*, page 27, lines 16-17 of the specification. Support for new claims 81-84 can be found on, *e.g.*, page 67, lines 28-30 of the specification. Support for new claim 85 can be found on, *e.g.*, page 27, line 28 to page 28, line 16 of the specification. Support for new claim 86 can be found on, *e.g.*, page 68, line 11 of the specification. Support for new claim 87 can be found on, *e.g.*, page 68, line 12 of the specification. Support for new claim 88 can be found on, *e.g.*, page 68, line 13 of the specification. Support for new claim 89 can be found on, *e.g.*, page 69, line 1 of the specification. Support for new claim 90 can be found on, *e.g.*, page 69, line 6 of the specification. No new matter has been introduced.

#### Interview

Applicant and Applicant's representative greatly appreciate the courtesy shown by Examiner Wessendorf in the November 13, 2000 interview and further appreciate her thoughtful consideration of arguments made during the interview.

#### The 112, First Paragraph, Rejection

Claims 30, 33, 67-69 and 70-75 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking a written description. According to the Office Action, "[t]he specification does not provide an adequate written description of the various components in order to practice the claimed method...[T]he claims cover too numerous undefined or

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incompletely described parameters besides the agent such as the target analyte, substrate, adsorbent, ligand or receptors, and more importantly, the conditions for the specific interactions of [the] different unspecified components to occur."

Applicants respectfully traverse this rejection. However, in the interest of expediting the prosecution, Applicants have canceled the rejected claims and replaced them with new claims 76-90. The language used to refer to various components in the screening method is simplified as discussed with the Examiner at the interview, and the physical relationship between various components have been further clarified. In particular, the claims now make clear that the interaction being examined is between a receptor and a ligand known to bind to each other. Written support for these terms are found on, for example, the section beginning on page 67, line 24 of the specification. Applicants believe that this amendment is sufficient to overcome any alleged lack of written description. Accordingly, withdrawal of the rejection is respectfully requested.

#### The 112, Second Paragraph, Rejection

Claims 30, 33, 67-69 and 70-75 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. As noted above, Applicants have canceled the rejected claims and replaced them with new claims 76-90. Applicants believe that the new claims are definite and overcome any alleged indefiniteness of the previously pending claims. Accordingly, withdrawal of the rejection is respectfully requested.

#### The Anticipation Rejection

Claims 30, 33, 36, 42, 49, 54, 63, 67, 68, 70 and 74 were rejected as allegedly being anticipated by Seigel *et al.* (Abstract, *J. Mass Spectrom.* 33: 264-273 (1998)). According to the Office Action, "[t]he claimed method of identifying an agent that modulates interaction between an adsorbent and a target analyte by adsorbing the target analyte to the adsorbent and detecting the interaction or modulation effect of the agent by spectrometry is fully met by the process of Seigel, as described in the abstract." See page 6 of the Office Action.

Applicants respectfully traverse this rejection. As an initial matter, Applicants note that the Seigel *et al.* publication was published after the effective filing date of the present

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application. It appears that the Examiner is not relying on the entire 1998 Seigel *et al.* publication in rejecting the claims, but is relying on its abstract with an assumption that the abstract is a fair representation of what was disclosed at the 44th ASMS Conference on Mass Spectrometry and Allied Topics, May 12-16, 1996, Portland, OR, and at the 45th ASMS Conference on Mass Spectrometry and Allied Topics, June 1-5, 1997, Palm Springs, CA (*see* the footnote at p. 264). Because the article indicates that only "preliminary reports" of the 1998 Seigel *et al.* publication have been presented at these meetings, it is unclear whether the abstract of the 1998 publication is a fair representation of what was described at the meetings. Accordingly, Applicants submit that the abstract of the 1998 publication cannot be relied upon as a prior art against the present claims, and the rejection should be withdrawn for this reason alone.

Even if the abstract in the 1998 publication were a fair representation of the disclosures at the meetings, the abstract does not anticipate the claimed invention. "For a prior art reference to anticipate in terms of 35 U.S.C. §102, every element of the claimed invention must be identically shown in a single reference." *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). Here, claims 76-90 are not anticipated, because every element of claim 76 (the only independent claim) is not identically shown in the abstract. For example, the abstract does not teach, *inter alia*, desorption spectrometry which comprises desorbing and ionizing a receptor which is *bound to the substrate-bound ligand* (or a ligand which is bound to the substrate-bound receptor). Rather, the abstract describes using electrospray ionization mass spectrometry in which none of the molecules (*e.g.*, an inhibitor or a protease) are bound to a substrate when they are ionized. As described at the carryover paragraph of pages 266 and 267 of Seigel *et al.*, the sample was prepared in a solvent and was infused into the electrospray mass spectrometer in the solution form. Therefore, every element of the present claims is not identically shown in the abstract. Accordingly, the abstract does not anticipate the claimed invention.

#### The Obviousness Rejection

Claims 30, 33, 36, 42, 46, 49, 54, 58, 63, 64, 67-69 and 70-75 were rejected under 35 U.S.C. §103(a) as allegedly being obvious over Siegel *et al.* in view of Kauvar (WO89/09088). According to the Office Action, "Siegel does not teach an antibody as the ligand, *i.e.*, adsorbent. However, Kauvar discloses a method of screening a polypeptide agent

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such as antibody and the use of paralogs *i.e.*, agent to inhibit binding of antibody to antigen. *See e.g.*, at *e.g.*, page 5, lines 23-31; page 14, lines 7-35. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use an antibody as the adsorbent in the method of Siegel, if one desires determining antibody-antigen reaction." *See* pages 7-8 of the Office Action.

As an initial matter, Applicants note that Kauvar's teachings described in the Office Action are inaccurate. The portions of Kauvar cited at page 7 of the Office Action do not teach or suggest screening an antibody or using paralogs as an agent to inhibit binding of antibody to antigen, as suggested by the Examiner. Rather, Kauvar describes using paralogs (*i.e.*, a peptide having 4-20 amino acids) as a substrate in affinity chromatography or as a substitute for antibodies in immunoassays (*see, e.g.*, abstract and page 6, lines 1-5). More specifically, Kauvar describes methods for designing and producing paralogs that have a specific affinity for a desired analyte so that the paralogs can be used as a substrate to bind the desired analyte (*see, e.g.*, pages 8-14). While Kauvar suggests using paralogs as a substitute for antibodies that bind the desired analyte, Kauvar does not teach or suggest using paralogs to inhibit binding of antibody to antigen. Therefore, Kauvar's disclosure is improperly relied upon by the Office Action in rejecting the claims.

Applicants respectfully traverse this rejection. Obviousness has not been established, because the cited references, alone or in combination, do not teach or suggest all the limitations of the claims. To establish *prima facie* obviousness, all of the claim limitations must be taught or suggested by the prior art. *In re Ryoka*, 180 USPQ 580 (CCPA 1974). *See, also*, MPEP §2143.03. In the instant case, neither the Siegel *et al.* abstract nor Kauvar teaches or suggests, *inter alia*, using desorption spectrometry which comprises desorbing and ionizing a receptor which is bound to a substrate-bound ligand (or a ligand which is bound to a substrate-bound receptor). As noted above, Siegel *et al.* uses electrospray ionization mass spectrometry in which none of the molecules are bound to any substrate when they are ionized. Rather, the molecules being ionized in Siegel *et al.* are in a solution. Kauvar does not cure this deficiency of Siegel *et al.* In fact, Kauvar does not teach or suggest using any type of mass spectrometry. Kauvar describes using methods such as X-ray film or gamma counter to detect binding between

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molecules (*see, e.g.*, page 17, line 35 to page 18, line 5). Therefore, Siegel *et al.* and Kauvar, alone or in combination, do not teach or suggest all the limitations of the claims.

Furthermore, one would not have been led to modify Siegel *et al.* in view of Kauvar in the manner suggested by the Examiner, because doing so would be contrary to the teachings of Siegel *et al.* A prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). In the instant case, page 8 of the Office Action states that "[o]ne would have been motivated to use spectrometric analysis coupled with adsorption chromatography since the combination of said two methods would obviously [result] in identifying or better characterization of a desired product." However, Siegel *et al.* teaches away from using affinity chromatography coupled with mass spectrometry. For example, Siegel *et al.* refers to the prior publications by Dr. Hutchens (a co-inventor of the present application) and states the following:

A unique application of affinity chromatography coupled to mass spectrometry is illustrated by the use of probe tips prepared with bound antibodies or proteins to select specific components from biological fluids.<sup>29-35</sup> \*\*\* *These affinity chromatographic techniques may not be very rapid or sensitive, and the preparation of columns, tips, chips and fibers may not be trivial.* (Emphasis added). *See* page 265, column 1, third paragraph of Siegel *et al.*

This and other passages in Siegel *et al.* clearly suggest that electrospray methods are preferred for the study of protein interactions and specifically recommend against the use of substrate-bound receptors in mass spectrometry methods, as claimed here. Therefore, Siegel *et al.* teach away from a combination with Kauvar (which is relied upon by the Examiner for disclosure of affinity chromatography). Therefore, one would not have been led to modify Siegel *et al.* in view of Kauvar in the manner suggested by the Examiner.

For the above reasons, obviousness has not been established, and withdrawal of the rejection is respectfully requested.

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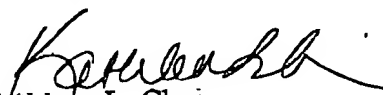
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CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

  
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